Dextromethorphan, the dextro isomer of the methyl ether of laevorphanol, is structurally related to the opiates but is not a narcotic agent. Dextromethorphan has been claimed to possess several advantages over codeine. Thus, it is said to produce less gastrointestinal disturbance and to have no effect on sputum consistency and ciliary activity [34]. Respiratory depression is less likely than with codeine [35]. When accidental overdosage proves dangerous, naloxone may be a useful antidote [36]. Dextromethorphan was at one time widely claimed to be free from abuse potential [37]. However, drug regulatory authorities in several countries are receiving reports of abuse of the drug and calls have been made to reclassify the drug as a prescription-only item [38].

Dextromethorphan is one of the most thoroughly investigated antitussives and, like codeine, its effectiveness has been shown by both objective and subjective testing [39–40]. This has, however, not always been a consistent finding [15, 41].

A recent study [15] revealed that when dextromethorphan 30 mg, noscapine 30 mg and codeine phosphate 20 mg were tested for activity against citric acid-induced cough in normal subjects, only the codeine was statistically better than a placebo. There was, however, no statistical difference between codeine and dextromethorphan. When the numerous studies on dextromethorphan are pooled, the evidence indicates that dextromethorphan is an effective antitussive agent. It appears to be a weaker but safer antitussive than codeine. Dextromethorphan concentration in plasma can be modelled by a one-compartment model. Recent studies [42] have shown that, in the majority of patients, dextromethorphan is metabolized to dextrophan, with little unmetabolized dextromethorphan being detectable in the urine or plasma. Dextrophan had a half-life of about 2 hours in those individuals. In some patients, however, dextromethorphan with a half-life of about 12 hours is metabolized more slowly and dextrophan formed has a half-life of about 6 hours. In a third group, dextromethorphan is hardly metabolized and its half-life is prolonged to over 40 hours. This wide variability in metabolism, which can be classified into distinct groups, is referred to as polymorphism, a phenomenon also observed with drugs such as debrisoquine. A more recent study produced a bimodal distribution for extent of dextromethorphan metabolism [43]. Indeed, dextromethorphan has now been suggested as a probe for phenotyping [44]. Clearly, then, dextromethorphan's activity will show wide intersubject variability.

Diphenhydramine and antihistamines

Diphenhydramine is an interesting antihistamine in that some studies have shown it to be a useful antitussive [45–46]. The evidence for its effectiveness is not, however, as extensive as that for codeine and dextromethorphan. As with all centrally-acting antihistamines, diphenhydramine may cause drowsiness in some patients, while infants may shown paradoxical excitement [47]. The drying

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